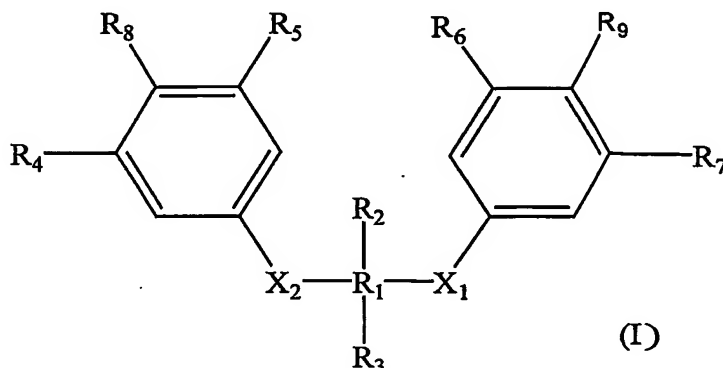


**WHAT IS CLAIMED:**

1. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (I):



wherein:

X<sub>1</sub> and X<sub>2</sub> are independently selected from the group consisting of oxy and a dialkyl substituted silyl;

R<sub>1</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl;

R<sub>2</sub> and R<sub>3</sub> are independently selected from the group consisting of H and a C<sub>1</sub>-C<sub>4</sub> alkyl;

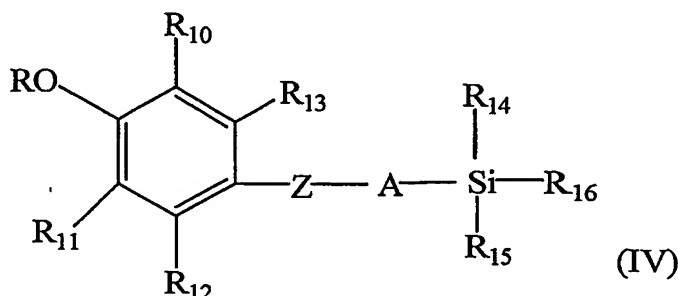
R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub> are independently selected from the group consisting of H, methoxy, and a branched or straight chain C<sub>1</sub>-C<sub>6</sub> alkyl; and

R<sub>8</sub> and R<sub>9</sub> are independently selected from the group consisting of hydrogen, hydroxy, trifluoromethyl, halide, amine, alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, -O(C<sub>1</sub>-C<sub>6</sub> alkyl), -OCO-(H or C<sub>1</sub>-C<sub>7</sub> alkyl), -OCO-(C<sub>3</sub>-C<sub>7</sub> alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C<sub>0</sub>-C<sub>8</sub> alkyl)-COOH, -(C<sub>2</sub>-C<sub>8</sub> alkenyl)-COOH, -OCO-(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, -OCO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH, -CO-(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, and -CO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH;

wherein when the R<sub>8</sub> or R<sub>9</sub> substituents are alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl, -O(C<sub>1</sub>-C<sub>6</sub> alkyl), -OCO-(H or C<sub>1</sub>-C<sub>7</sub> alkyl), -OCO-(C<sub>3</sub>-C<sub>7</sub> alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C<sub>0</sub>-C<sub>8</sub> alkyl)-COOH, -(C<sub>2</sub>-C<sub>8</sub> alkenyl)-COOH, -OCO-(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, -OCO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH, -CO-

(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, or -CO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH, they may be independently substituted with one or more functionalities independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, -OH, -OCH<sub>3</sub>, -OCH<sub>2</sub>CH<sub>3</sub>, halomethyl, dihalomethyl, trihalomethyl, -NH<sub>2</sub>, -NO<sub>2</sub>, -CN, -NC, -C(=NH)(-NH<sub>2</sub>), -SH, -COOH, -COOCH<sub>3</sub>, and -COOCH<sub>2</sub>CH<sub>3</sub>;

with the proviso that said compound of Formula (I) is not a compound of Formula (IV)



wherein:

R<sub>10</sub> and R<sub>15</sub> are each independently C<sub>1</sub> - C<sub>6</sub> alkyl;

R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are each independently hydrogen or C<sub>1</sub> - C<sub>6</sub> alkyl;

R is hydrogen or -C(O)-(CH<sub>2</sub>)<sub>m</sub>-Q, wherein Q is hydrogen or -COOH and m is an integer 1, 2, 3 or 4;

Z is a thio, oxy or methylene group;

A is a C<sub>1</sub> - C<sub>4</sub> alkylene group;

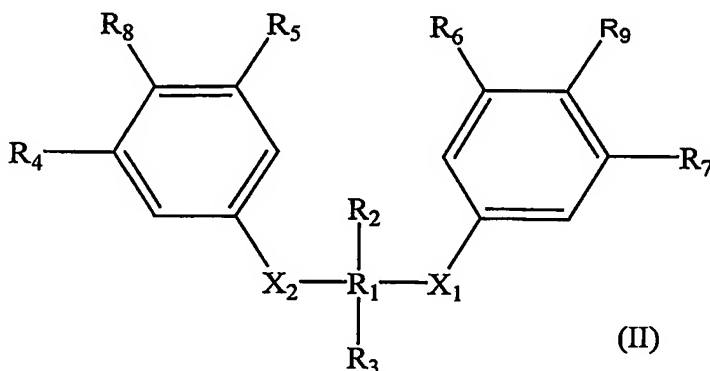
R<sub>14</sub> and R<sub>16</sub> are each independently a C<sub>1</sub> - C<sub>6</sub> alkyl or -(CH<sub>2</sub>)<sub>n</sub>-(Ar), wherein n is an integer 0, 1, 2 or 3; and Ar is phenyl or naphthyl unsubstituted or substituted with one to three substituents selected from the group consisting of hydroxy, methoxy, ethoxy, halogen, trifluoromethyl, C<sub>1</sub> - C<sub>6</sub> alkyl, or -NR<sub>17</sub> R<sub>18</sub>, wherein R<sub>17</sub> and R<sub>18</sub> are each independently hydrogen or C<sub>1</sub> - C<sub>6</sub> alkyl; with the proviso that when R<sub>11</sub> and at least one of R<sub>14</sub> or R<sub>16</sub> is C<sub>1</sub> - C<sub>6</sub> alkyl, and Ar is not substituted with trifluoromethyl or -NR<sub>17</sub> R<sub>18</sub>, then R is -C(O)-(CH<sub>2</sub>)<sub>m</sub>-Q; or a pharmaceutically acceptable salt thereof.

2. The method of claim 1, wherein X<sub>1</sub> and X<sub>2</sub> are independently selected from the group consisting of oxy and dimethyl-silyl; R<sub>1</sub> is methylene; R<sub>2</sub> and R<sub>3</sub> are hydrogen, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub> are independently selected from the group consisting of

hydrogen and tert-butyl; and  $R_8$  and  $R_9$  are independently selected from the group consisting of hydroxy and methoxy.

3. The method of claim 1, wherein  $R_4$  and  $R_5$  are tert-butyl, and  $R_8$  is hydroxy.

5 4. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (II):



10 wherein

$X_1$  and  $X_2$  are independently selected from the group consisting of thio, oxy, and a dialkyl substituted silyl;

$R_1$  is  $C_1$ - $C_4$  alkyl;

15  $R_2$  and  $R_3$  are independently selected from the group consisting of H and a  $C_1$ - $C_4$  alkyl;

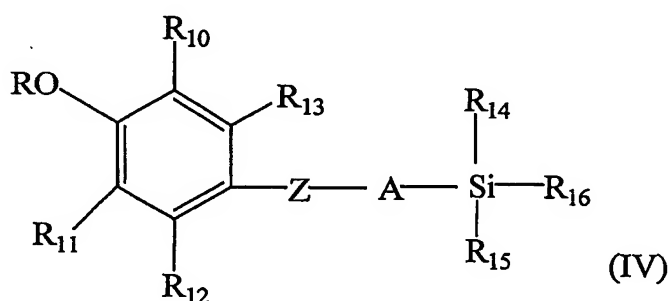
$R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  are independently selected from the group consisting of H, methoxy, and a branched or straight chain  $C_1$ - $C_6$  alkyl; and

20  $R_8$  and  $R_9$  are independently selected from the group consisting of hydrogen, hydroxy, trifluoromethyl, halide, amine, alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl,  $-O(C_1$ - $C_6$  alkyl),  $-OCO$ -(H or  $C_1$ - $C_7$  alkyl),  $-OCO$ -( $C_3$ - $C_7$  alkenyl),  $-OCO$ -(aryl),  $-OCO$ -(heteroaryl),  $-(C_0$ - $C_8$  alkyl)- $COOH$ ,  $-(C_2$ - $C_8$  alkenyl)- $COOH$ ,  $-OCO$ -( $C_0$ - $C_6$  alkyl)- $COOH$ ,  $-OCO$ -( $C_2$ - $C_6$  alkenyl)- $COOH$ ,  $-CO$ -( $C_0$ - $C_6$  alkyl)- $COOH$ , and  $-CO$ -( $C_2$ - $C_6$  alkenyl)- $COOH$ ;

25 wherein when the  $R_8$  or  $R_9$  substituents are alkyl, alkenyl, aryl, heteroaryl, alkanoyl, aryloyl, heteroaryloyl,  $-O(C_1$ - $C_6$  alkyl),  $-OCO$ -(H or  $C_1$ - $C_7$  alkyl),  $-OCO$ -

(C<sub>3</sub>-C<sub>7</sub> alkenyl), -OCO-(aryl), -OCO-(heteroaryl), -(C<sub>0</sub>-C<sub>8</sub> alkyl)-COOH, -(C<sub>2</sub>-C<sub>8</sub> alkenyl)-COOH, -OCO-(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, -OCO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH, -CO-(C<sub>0</sub>-C<sub>6</sub> alkyl)-COOH, or -CO-(C<sub>2</sub>-C<sub>6</sub> alkenyl)-COOH, they may be independently substituted with one or more functionalities independently selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, -OH, -OCH<sub>3</sub>, -OCH<sub>2</sub>CH<sub>3</sub>, halomethyl, dihalomethyl, trihalomethyl, -NH<sub>2</sub>, -NO<sub>2</sub>, -CN, -NC, -C(=NH)(-NH<sub>2</sub>), -SH, -COOH, -COOCH<sub>3</sub>, and -COOCH<sub>2</sub>CH<sub>3</sub>;

with the proviso that when said compound of Formula (II) is not a compound of Formula (IV)



wherein:

R<sub>10</sub> and R<sub>15</sub> are each independently C<sub>1</sub> - C<sub>6</sub> alkyl;

R<sub>11</sub>, R<sub>12</sub> and R<sub>13</sub> are each independently hydrogen or C<sub>1</sub> - C<sub>6</sub> alkyl;

R is hydrogen or -C(O)-(CH<sub>2</sub>)<sub>m</sub>-Q, wherein Q is hydrogen or -COOH and

m is an integer 1, 2, 3 or 4;

Z is a thio, oxy or methylene group;

A is a C<sub>1</sub> - C<sub>4</sub> alkylene group;

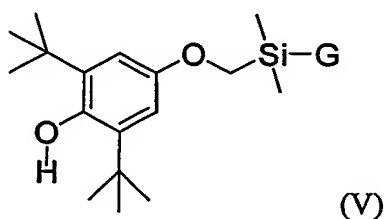
R<sub>14</sub> and R<sub>16</sub> are each independently a C<sub>1</sub> - C<sub>6</sub> alkyl or -(CH<sub>2</sub>)<sub>n</sub>-(Ar), wherein n is an integer 0, 1, 2 or 3; and Ar is phenyl or naphthyl unsubstituted or substituted with one to three substituents selected from the group consisting of hydroxy, methoxy, ethoxy, halogen, trifluoromethyl, C<sub>1</sub> - C<sub>6</sub> alkyl, or -NR<sub>17</sub>R<sub>18</sub>, wherein R<sub>17</sub> and R<sub>18</sub> are each independently hydrogen or C<sub>1</sub> - C<sub>6</sub> alkyl; with the proviso that when R<sub>11</sub> and at least one of R<sub>14</sub> or R<sub>16</sub> is C<sub>1</sub> - C<sub>6</sub> alkyl, and Ar is not substituted with trifluoromethyl or -NR<sub>17</sub>R<sub>18</sub>, then R is -C(O)-(CH<sub>2</sub>)<sub>m</sub>-Q; or a pharmaceutically acceptable salt thereof.

5. The method of claim 4, wherein  $X_1$  and  $X_2$  are independently selected from the group consisting of thio and dimethyl-silyl;  $R_1$  is methylene;  $R_2$  and  $R_3$  are independently selected from the group consisting of hydrogen and methyl;  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  are independently selected from the group consisting of hydrogen and tert-butyl; and  $R_8$  and  $R_9$  are independently selected from the group consisting of hydrogen, hydroxy, methoxy, and butandioate; with the proviso that when  $X_1$  and  $X_2$  are both thio,  $R_8$  and  $R_9$  are not both hydroxy.

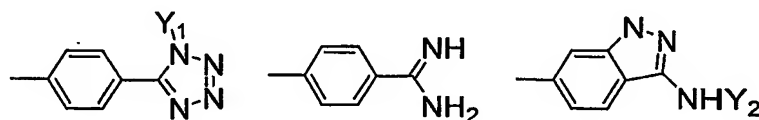
6. The method of claim 4, wherein  $R_4$  and  $R_5$  are tert-butyl, and  $R_8$  is hydroxy.

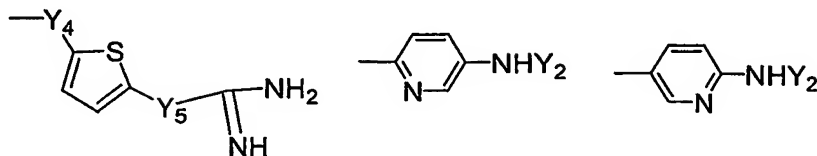
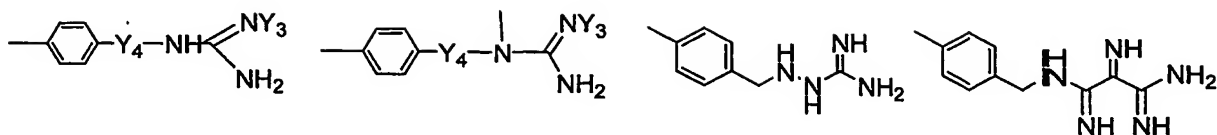
7. The method of claim 4, wherein  $X_1$  and  $X_2$  are thio;  $R_1$  is methylene;  $R_2$  and  $R_3$  are methyl;  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  are tert-butyl;  $R_8$  is hydroxy; and  $R_9$  is butandioate.

8. A method for the prophylactic or therapeutic treatment of a disease or disorder associated with vascular health, said method comprising administering to a subject in need of such treatment an amount effective to treat a disease or disorder associated with vascular health, of a compound of Formula (V):

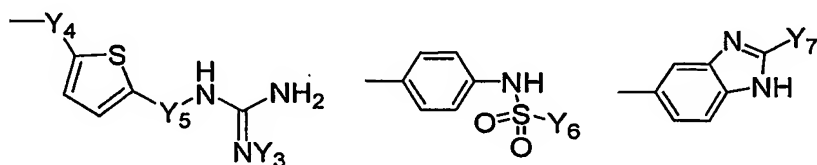
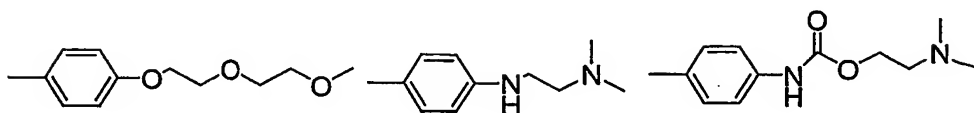


wherein G is selected from the group consisting of:

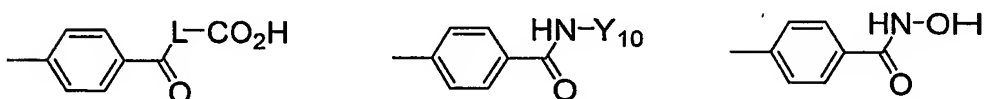




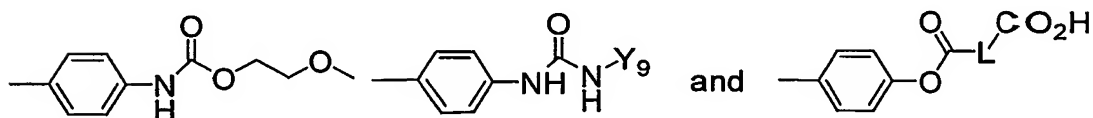
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10



15



wherein:

Y<sub>1</sub> is -H, C<sub>1</sub>-C<sub>4</sub> alkyl, or C<sub>3</sub>-C<sub>6</sub> alkenyl;

20 Y<sub>2</sub> is -H, C<sub>1</sub>-C<sub>4</sub> alkyl, or C<sub>3</sub>-C<sub>6</sub> alkenyl, aryl, heteroaryl, aryloyl, alkanoyl, or heteroaryloyl;

Y<sub>3</sub> is -H, -CN, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, aryl or heteroaryl;Y<sub>4</sub> is (CH<sub>2</sub>)<sub>n</sub>, where n is 0-4, or C<sub>2</sub>-C<sub>6</sub> alkenyl;Y<sub>5</sub> is NH, (CH<sub>2</sub>)<sub>n</sub>, where n is 0-4, or C<sub>2</sub>-C<sub>6</sub> alkenyl;

25 Y<sub>6</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

Y<sub>7</sub> is H, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or NH Y<sub>8</sub>;

$Y_8$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

$Y_9$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, or heteroaryl;

$Y_{10}$  is alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;

L is  $C_1$ - $C_6$  alkyl or  $C_2$ - $C_6$  alkenyl; and

- 5        wherein G may be additionally substituted with one or more substituents independently selected from the group consisting of -F, -Cl, -Br, -I, -NH<sub>2</sub>, -OH, -CN, -SH, -CH<sub>3</sub>, -CH<sub>2</sub>CH<sub>3</sub>, -CF<sub>3</sub>, -OCH<sub>3</sub>, -OCH<sub>2</sub>CH<sub>3</sub>, -COOH, -COOCH<sub>3</sub>, and -COOCH<sub>2</sub>CH<sub>3</sub>.

9.        A method according to any of claims 1 to 8, wherein said disease or  
10        disorder associated with vascular health is selected from the group consisting of: major adverse cardiac events, vascular access dysfunction, and male erectile dysfunction.

10.       A method according to any of claims 1 to 9, wherein said subject is  
15        selected from the group consisting of a hemodialysis patient, an end stage renal disease patient, or a diabetic patient.

11.       A method according to any of claims 1 to 10, wherein said subject is a subject having an increased oxidative burden or elevated oxidative stress, a subject having a vascular access shunt or graft, or a subject suffering from diabetes and experiencing erectile dysfunction or seeking prophylactic therapy.

- 20        12.       A method according to any of claims 1 to 11, wherein said subject is a human.

13.       A method according to any of claims 1 to 12, wherein said compound is administered to the subject orally.

- 25        14.       A method according to any of claims 1 to 13, wherein about 1mg to about 10g of said compound is administered per day to said subject in single, divided, or continuous doses to achieve a blood plasma concentration of said compound which is therapeutically effective in said treatment.

15. A method according to any of claims 1 to 13, wherein about 0.1g to about 3g of said compound is administered per day to said subject in single, divided, or continuous doses to achieve a blood plasma concentration of said compound which is prophylactically effective in said treatment.

5 16. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is a major adverse cardiac event.

17. The method of claim 16, wherein said subject is a subject having an increased oxidative burden or elevated oxidative stress.

10 18. The method of claim 16, wherein treatment includes a reduction in the risk of occurrence of said major adverse cardiac event.

19. The method of claim 16, wherein said method comprises identifying a subject as having an increased oxidative burden or elevated oxidative stress.

20. The method of claim 16, wherein said subject has normal or normalized lipid levels.

15 21. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is vascular access dysfunction.

22. The method of claim 21, wherein said subject is a hemodialysis patient and said compound is administered directly following hemodialysis.

20 23. The method of claim 21, wherein said subject suffers from end stage renal disease.

24. The method of claim 21, wherein said vascular access dysfunction is associated with arteriovenous shunt stenosis.

25. A method according to any of claims 1 to 8, wherein said disease or disorder associated with vascular health is erectile dysfunction.

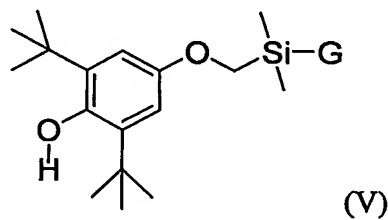
25 26. The method of claim 25, wherein said subject is a diabetic suffering from erectile dysfunction.



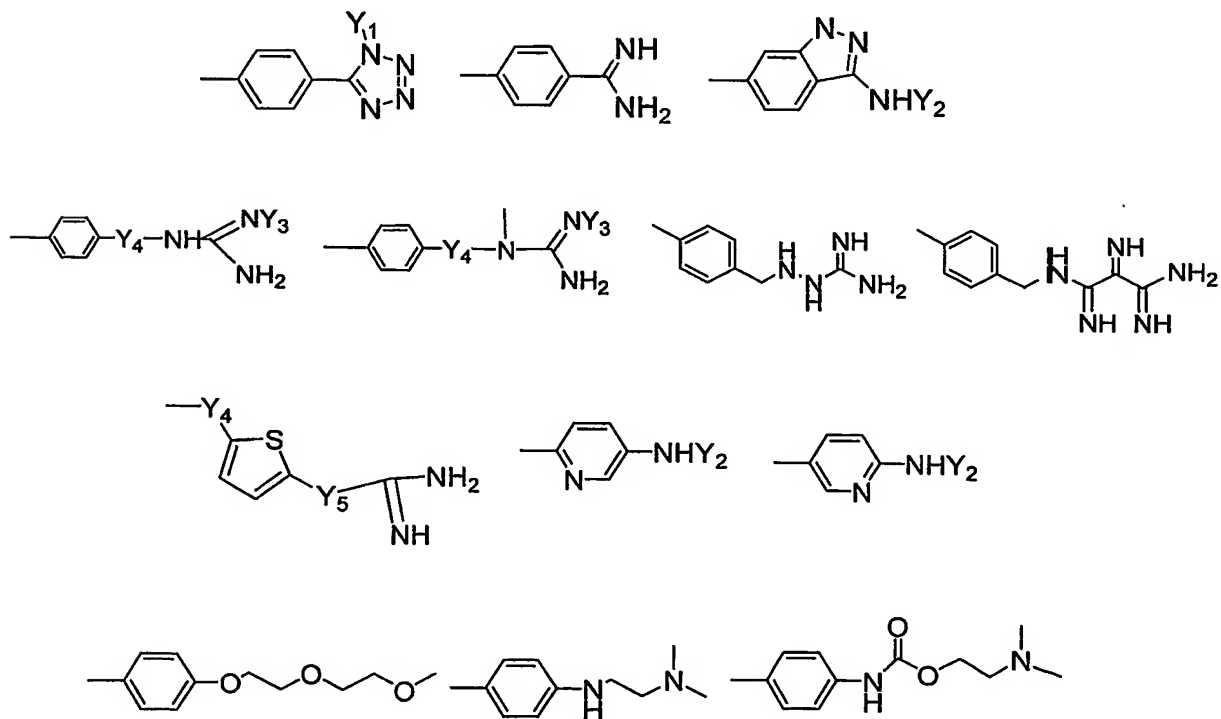
27. The method of claim 25, wherein said treatment is given prophylactically.

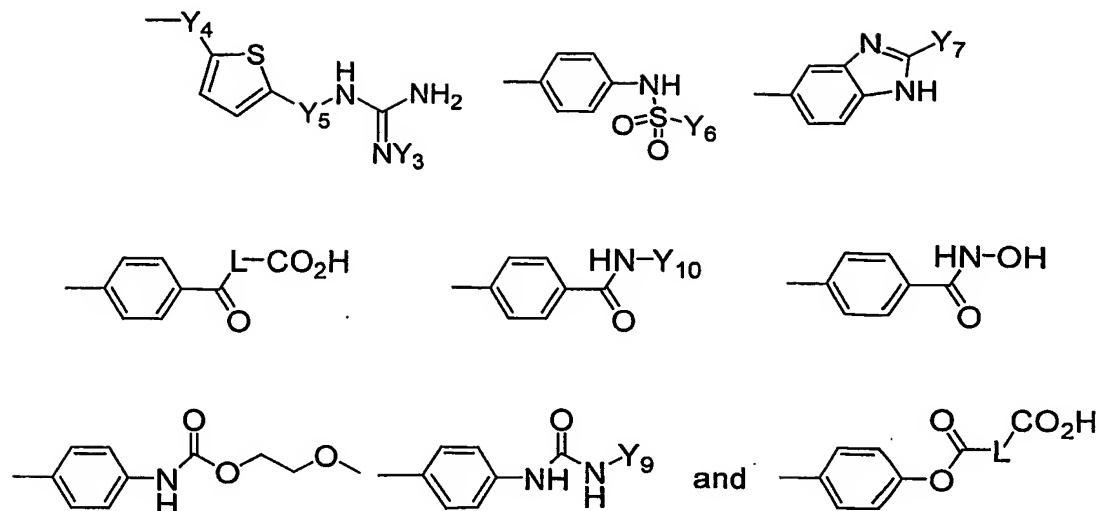
28. The method of claim 25, wherein said treatment is a combination treatment comprising a phosphodiesterase inhibitor as a second active ingredient.

29. A pharmaceutical composition comprising a compound of Formula (V), or a salt or hydrochloride thereof,



wherein G is selected from the group consisting of:





wherein:

- 10  $Y_1$  is  $-H$ ,  $C_1$ - $C_4$  alkyl, or  $C_3$ - $C_6$  alkenyl;  
 $Y_2$  is  $-H$ ,  $C_1$ - $C_4$  alkyl, or  $C_3$ - $C_6$  alkenyl, aryl, heteroaryl, aryloyl, alkanoyl, or heteroaryloyl;  
 $Y_3$  is  $-H$ ,  $-CN$ ,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl or heteroaryl;  
 $Y_4$  is  $(CH_2)_n$ , where  $n$  is 0-4, or  $C_2$ - $C_6$  alkenyl;  
15  $Y_5$  is  $NH$ ,  $(CH_2)_n$ , where  $n$  is 0-4, or  $C_2$ - $C_6$  alkenyl;  
 $Y_6$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;  
 $Y_7$  is  $H$ ,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl, or  $NH$   $Y_8$ ;  
 $Y_8$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;  
20  $Y_9$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  alkenyl, aryl, or heteroaryl;  
 $Y_{10}$  is alkyl, aryl, heteroaryl, alkylaryl, or alkylheteroaryl;  
 $L$  is  $C_1$ - $C_6$  alkyl or  $C_2$ - $C_6$  alkenyl; and  
wherein  $G$  may be additionally substituted with one or more substituents independently selected from the group consisting of  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-NH_2$ ,  $-OH$ ,  $-CN$ ,  $-SH$ ,  $-CH_3$ ,  $-CH_2CH_3$ ,  $-CF_3$ ,  $-OCH_3$ ,  $-OCH_2CH_3$ ,  $-COOH$ ,  $-COOCH_3$ , and  $-COOCH_2CH_3$ ;  
25 and a pharmaceutically acceptable excipient.

30. The pharmaceutical composition of claim 29, wherein said compounds of Formula (V) are formulated for oral administration in a self-emulsifying drug delivery system.

31. The pharmaceutical composition of claim 29, further comprising one or members of the group consisting of lactose, calcium phosphate, kaolin, glycerin, propylene glycol, polyethylene glycol, peanut oil, liquid paraffin, olive oil, sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth, gum acacia; dispersing agents, wetting agents, and thickening agents.

32. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of major adverse cardiac events.

33. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of vascular access dysfunction.

34. The pharmaceutical composition of any one of claims 29 to 31, further comprising one or more other active ingredients useful in the prophylactic or therapeutic treatment of erectile dysfunction.